

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference CL001471 PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2004/017654	International filing date (<i>day/month/year</i>) 04 June 2004 (04.06.2004)	Priority date (<i>day/month/year</i>) 04 June 2003 (04.06.2003)	
International Patent Classification (IPC) or national classification and IPC ⁷ C07C 311/18, 311/54, A61K 31/41, 31/18, 31/38, A61P 29/02, 25/28, 37/02, 35/00, 9/10, C07D 263/56, 335/02, A61P 17/06			
Applicant AXYS PHARMACEUTICALS			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the report
<input checked="" type="checkbox"/>	Box No. II	Priority
<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 740 14 35</p>	<p>Date of issuance of this report 08 December 2005 (08.12.2005)</p> <p>Authorized officer Masashi Honda</p> <p>Telephone No. +41 22 338 70 10</p>
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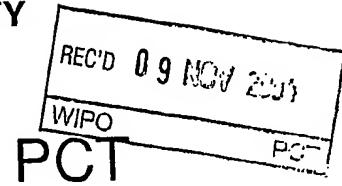
PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

16/12



WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

		Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US2004/017654	International filing date (day/month/year) 04.06.2004	Priority date (day/month/year) 04.06.2003
International Patent Classification (IPC) or both national classification and IPC C07C311/18, C07C311/54, A61K31/41, A61K31/18, A61K31/38, A61P29/02, A61P25/28, A61P37/02, A61P35/00,		
Applicant AXYS PHARMACEUTICALS		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:  European Patent Office - Gitschner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Rufet, J Telephone No. +49 30 25901-332
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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/017654

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,

claims Nos. 1-11, 13, 15-18 all partially and 19,20 in respect with industrial applicability because:

the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the whole application or for said claims Nos. 1-11, 13, 15-18 all partially and 19,20 with respect to industrial applicability

the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form has not been furnished
 does not comply with the standard

the computer readable form has not been furnished
 does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/017654

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-20
	No: Claims	
Inventive step (IS)	Yes: Claims	1-20
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	19,20

2. Citations and explanations

see separate sheet

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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Re Item III.

1. Claims 19, 20 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. Present claims 1-11, 13, 15-18 relate to an extremely large number of possible compounds and compositions thereof, due to the use of speculative expressions in those claims like: "alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocycll etc.. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful examination over the whole of the scope is impossible. Consequently, the examination has only been carried out for those parts of claims which appear to be supported and disclosed (Art. 34(4)(a)(ii) PCT) and which have been searched (Rule 66.1(e) PCT), namely those parts relating to the compounds of formula (Ia) or (Ib) wherein the speculative expressions in the different substituents of claim 1 have been limited to their respective definitions given in the description p. 6 to p. 12, line 14 with R3 according to claim 17.

The Applicant is advised that the EPO cannot normally carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any International Preliminary Examination procedure.

Re Item V.

The following documents are referred to in this communication:

D1: WO 03/029200 A
D2: WO 01/19816 A
D3: WO 00/51998 A
D4: EP 0 623 627 A
D5: WO 02/069901 A
D6: WO 01/19796 A

1. Documents D1 and D2 are considered to represent equally the most relevant state of

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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the art and disclose compounds according to formula (Ia) or (Ib) of present claim 1, which differ by the nature of the substituent R⁴, which corresponds to substituent R⁶ in D1, D2.

Documents D3-D6 refer to similar compounds useful as cysteine protease inhibitors which do not have an amidino moiety in their structure.

The subject-matter of claims 1-20 as searched is therefore novel (Article 33(2) PCT).

2. In view of the teaching of the closest prior art D1/D2, the problem to be solved by the present invention may be regarded as the provision of further cysteine protease inhibitors.

The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons: In view of the examples and the biological examples given in page 65-67 it is credible that the problem as defined above has actually been solved by the technical features of the claimed compounds.

For a skilled person, in view of the teaching of the closest prior art D1-D2 (e.g. see D1, claim 19, compounds with A15-38, A52-57, A88-97 or A105-108) and taking into account the significant structural difference between the claimed compounds and those of the prior art D1-D6, the proposed solution to the abovementioned problem was not foreseeable. In other words, there is no indication in D1-D2 nor in D3-D6 to use a benzenesulfonyl group as a possible substituent for the amidino group already known from D1-D2. Consequently claims 1-20 meet the criteria of Art. 33 (3) PCT.

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